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Lung Cancer in Mayak Workers

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The cohort of nuclear workers at the Mayak Production Association, located in the Russian Federation, is a unique resource for providing information on the health effects of exposure to plutonium as well as the effects of protracted external dose. Lung cancer mortality risks were evaluated in 21,790 Mayak workers, a much larger group than included in previous evaluations of lung cancer risks in this cohort. These analyses, which included 655 lung cancer deaths occurring in the period 1955–2000, were the first to evaluate both excess relative risk (ERR) and excess absolute risk (EAR) models and to give detailed attention to the modifying effects of gender, attained age and age at hire. Lung cancer risks were found to be significantly related to both internal dose to the lung from plutonium and external dose, and risks were described adequately by linear functions. For internal dose, the ERR per gray for females was about four times higher than that for males, whereas the EAR for females was less than half that for males; the ERR showed a strong decline with attained age, whereas the EAR increased with attained age until about age 65 and then decreased. Parallel analyses of lung cancer mortality risks in Mayak workers and Japanese A-bomb survivors were also conducted. Efforts currently under way to improve both internal and external dose estimates, and to develop data on smoking, should result in more accurate risk estimates in the future.

INTRODUCTION

During the early period of operation of the Mayak nuclear facility, which is located in the Chelyabinsk region of the Russian Federation, many workers were exposed to inhaled plutonium at levels much higher than those considered permissible today. A large number of these workers were also exposed to doses of external γ radiation that were substantially higher than current occupational dose limits. Although workers exposed to plutonium in facilities in the United States and United Kingdom have been studied (*1–4*), the level of the exposures and the small number of workers who have received such exposure greatly limit what can be learned about plutonium-related health effects. Because of these limitations, quantitative estimates of risks from exposure to plutonium have been obtained either from studies of persons exposed to other α-particle-emitting radionuclides or by applying a radiation weighting factor to estimates obtained from Japanese atomic bomb survivors exposed to low-LET radiation (*5, 6*). The Mayak worker cohort is a unique resource for providing information on the health effects of exposure to plutonium as well as the effects of protracted external dose.

Several papers have evaluated cancer risks in Mayak workers. Recently Shilnikova *et al.* (*7*) analyzed risks of solid cancer and leukemia with emphasis on the effects of external exposure. From both human and experimental animal data, it is known that the lung, bone and liver receive the largest doses from inhaled plutonium (*5, 6*). Koshurnikova *et al.* (*8*) and Gilbert *et al.* (*9*) conducted a preliminary evaluation of risks of bone and liver cancer in relation to plutonium exposure, and several previous papers have evaluated lung cancer risks. These include both case–control (*10*, *11*) and cohort studies (*12–14*). The cohort studies focused on a relatively small subgroup of male workers initially employed before 1959 for whom quantitative estimates of doses to the lung from plutonium were available.

The current paper provides a comprehensive evaluation of lung cancer risks with detailed attention to both internal dose to the lung from plutonium and external dose. Unlike previous papers on lung cancer risks, these analyses include all workers who were initially employed in the period 1948–1972 in either the main or auxiliary plants, explore both excess relative risk and excess absolute risk models, and evaluate modification of risk by gender, attained age, age at hire, and time since exposure.

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TABLE 1
Number of Mayak Workers and Lung Cancer Deaths (in parentheses) by Plant, Plutonium Monitoring Status, Sex, Year of Hire, Age at Hire, and External Dose: Mean External and Internal Lung Dose by Sex, Year of Hire, Age at Hire, and External Dose

				Radiochemical and plutonium plants			All workers
	All workers	Auxiliary plants	Reactor plants	Not monitored for plutonium	Monitored for plutonium	Mean internal lung dose among monitored (Gy)	Mean external dose[a] (Gy)
Total	21,790 (655)	2582 (54)	4493 (131)	8856 (252)	5859 (218)	0.26	0.80
By sex							
Males	16,458 (594)	2084 (54)	3505 (124)	6724 (224)	4145 (192)	0.21	0.80
Females	5332 (61)	498 (0)	988 (7)	2132 (28)	1714 (26)	0.38	0.82
By year of hire							
1948–1953	9338 (436)	740 (25)	2457 (91)	4058 (171)	2083 (149)	0.55	1.47
1954–1958	4290 (134)	417 (17)	751 (22)	1912 (52)	1210 (43)	0.16	0.51
1959–1963	4364 (61)	573 (6)	702 (12)	1829 (25)	1260 (18)	0.09	0.23
1964–1972	3798 (24)	852 (6)	583 (6)	1057 (4)	1306 (8)	0.037	0.12
By age at hire							
15–19	8061 (130)	1123 (10)	1346 (23)	3405 (52)	2187 (45)	0.14	0.63
20–29	10,076 (359)	993 (23)	2442 (83)	3844 (125)	2797 (128)	0.34	0.93
30–39	2540 (120)	320 (14)	494 (16)	1030 (51)	696 (39)	0.34	0.88
40+	1113 (46)	146 (7)	211 (9)	577 (24)	179 (6)	0.11	0.71
By external dose							
Not monitored	4472 (91)	1273 (26)	520 (8)	2007 (45)	672 (12)	0.058	—
<0.1 Gy	4744 (76)	811 (16)	841 (9)	1874 (31)	1218 (20)	0.072	0.04
0.1–1 Gy	8212 (221)	467 (12)	2315 (70)	3079 (79)	2351 (60)	0.17	0.39
1+ Gy	4362 (267)	31 (0)	817 (44)	1896 (97)	1618 (126)	0.61	2.41

[a] Among those monitored for external dose.

MATERIALS AND METHODS

This record-based epidemiological study required no contact with the cohort members. The project was reviewed and approved by the Institutional Review Boards of the Southern Urals Biophysics Institute and the Radiation Effects Research Foundation. It was exempted from such review at the National Cancer Institute (NCI) because NCI used only anonymized data.

The Study Population and Follow-up

The Mayak worker cohort and methods of follow-up have been described in detail elsewhere (*7, 15*). The main plants of the Mayak nuclear facility, which began operations in 1948, include nuclear reactors, a radiochemical plant, and a plutonium production facility, but only workers in the latter two facilities have the potential for exposure to plutonium. The original cohort included about 18,000 persons who were initially employed in one or more of these main plants in the years 1948–1972. About 2800 persons who worked only in the auxiliary plants (water treatment facility and mechanical repair plant) were recently added to the Mayak cohort to expand the number of workers with little or no radiation exposure. Table 1 shows the distribution of the 21,790 workers and 655 lung cancer deaths in the expanded cohort by sex, year of hire, age at hire, and external dose, and also by plant and whether or not they were monitored for plutonium. Also shown are mean internal lung doses for those monitored for plutonium (see below). About 24% of the workers were female, 43% were hired before 1954, and 37% were under age 20 at hire. Vital status is known for 90% of the cohort. By December 31, 2000, 8493 workers had died, and the cause of death was known for 8213 (97%) of these deaths.

Dosimetry

The Mayak Workers Registry includes annual external doses estimated from individual film badge monitoring data, maintained since 1948 by the Radiation Safety Service of the Mayak plant. The external monitoring program was designed to include all workers with a potential for external exposure, and about 80% of workers in the registry have external monitoring data.

Monitoring for plutonium exposure has been carried out at the Southern Urals Biophysics Institute (SUBI) since the late 1960s. Estimates of body burden and of doses from plutonium used in this paper are based on plutonium levels observed in urine collected over a 3-day period after a period of at least 30 days with no potential exposure (usually after vacation). This procedure avoided the influence of short-term clearance processes on the urinary excretion, but it results in some distortion of the plutonium kinetics (*16*). Although about 500 workers were monitored before 1970, the median date of monitoring was 1982. As of the end of 1995, about 31% of those who worked in the radiochemical or plutonium production plants had been monitored using this approach; extensive efforts beginning in 1996 to monitor additional workers have raised this to 40%. Scientists at SUBI formulated a mathematical model of the behavior of plutonium in the body based on their measurements of plutonium α-particle activity in urine and in body tissues at autopsy. In addition, the model considers the worker's occupational history and the physiochemical form of the plutonium aerosols (*17–19*). This model has been used to estimate annual equivalent dose to organs for each year of follow-up. Analyses in this paper are based on the estimated dose to the lung, which, for simplicity, is often referred to as ''internal dose''. As a result of collaborative work of Russian and U.S. dosimetrists, improvements have been made in the original SUBI model (*20*), and lung dose estimates used in this paper reflect these improvements.

TABLE 2
Number of Mayak Workers, Number Monitored for Plutonium, Distribution by Estimated Internal Lung Dose from Plutonium, Mean Internal Lung Dose, and Mean Body Burden, by Plutonium Surrogate Category[a]

		Plutonium surrogate category					
	Total	0	1	2	3	4[b]	5[b]
Total	21,790	7075	6861	5239	1702	250	663
Not monitored for plutonium	15,597	6741	3764	3319	1172	158	443
Total monitored (percent)	6193 (28)	334 (4.7)	3097 (45)	1920 (37)	530 (31)	92 (37)	220 (33)
By estimated internal lung dose							
Below detection limit	1560	214	984	267	79	4	12
>0–0.2 Gy	3688	116	1926	1330	233	34	49
0.2–1.0 Gy	688	4	172	273	163	20	56
1.0–3.0 Gy	163	0	13	39	46	20	45
3.0–5.0 Gy	39	0	1	9	4	5	20
5.0+ Gy	55	0	1	2	5	9	38
Mean internal lung dose (Gy)	0.24	0.016	0.058	0.16	0.40	1.89	2.91
Mean body burden (kBq)	1.84	0.45	0.51	1.58	2.67	14.3	17.8

[a] Plutonium surrogate categories are as follows: 0 = reactors and auxiliary plant workers hired in any period; 1 = main departments of the plutonium plant, hired 1964–1972, or auxiliary departments of the plutonium plant hired 1959–1972 or radiochemical plant, hired 1954–1972; 2 = main departments of the plutonium plant, hired 1959–1963 or auxiliary departments of the plutonium plant, hired 1950–1958 or radiochemical plant, hired 1948–1953; 3 = main departments of the plutonium plant, hired 1954–1958 or auxiliary departments of the plutonium plant, hired 1948–1949; 4 = main departments of the plutonium plant hired 1950–1953; 5 = main departments of the plutonium plant hired 1948–1949.

[b] Categories 4 and 5 were combined in dose–response analyses due to the small number of workers in these categories.

To make it possible to use the full cohort including workers in the radiochemical and plutonium plants for whom plutonium monitoring data are not available (for the purposes of evaluating the effects of external exposure), we developed a categorical surrogate index of plutonium exposure based on occupational history data, including work locations, starting dates, measured body burden values, and expert knowledge of working conditions at various times in the different facilities (*7*). Table 2 shows the definitions of the plutonium surrogate categories used by Shilnikova *et al.* (*7*) and in this paper along with the mean internal lung doses and body burdens among workers in each category who were monitored for plutonium. The table also shows the distribution by lung dose of monitored workers in each category. Both lung dose and body burden increase with surrogate category. However, the distributions by lung dose make it clear that there is considerable variability among monitored workers within a given surrogate index level. Because workers thought to have been at risk of exposure to the highest levels of plutonium were more likely to be selected for monitoring, the mean lung dose for monitored workers within a surrogate category cannot be regarded as a representative value for all workers in that category. Thus unmonitored workers in surrogate categories 1–5 are not considered to have internal lung doses that could be estimated and are not used for quantifying the plutonium dose response. However, the surrogate makes it possible to include the full cohort for evaluating the effects of external dose and for estimating the attributable risk from plutonium exposure.

Statistical Methods

The statistical methods employed in this paper are similar to those used in recent analyses of the Mayak worker data by Shilnikova *et al.* (*7*). Analyses were based on Poisson regression methods, where it is assumed that the number of deaths from the cause of interest is a Poisson variable with mean given by the product of the person-years and the cause-specific mortality rate for each cell of a multi-way person-year table. Analyses were implemented with the AMFIT module of the software package EPICURE (*21*).

Person-year tables were classified by plant (auxiliary plants, reactors, radiochemical plant, plutonium production plant), gender, plutonium surrogate index categories (see Table 2), attained age (5-year categories), age at hire (5-year categories), birth cohort (1885–1914, 1915–1924, 1925–1934, 1935–1955), calendar period (1948–1972, 1973–2000), plutonium monitoring status, cumulative internal dose to the lung, and cumulative external dose. Supplementary analyses with finer stratification on birth cohort and calendar period also were conducted. Attained age and calendar year refer to a worker's age or calendar year in a specified follow-up interval, and a given worker can contribute to several categories as he/she is followed over time. Plant, the plutonium surrogate, plutonium monitoring status, and cumulative doses were also treated as dependent on time. For plant and the plutonium surrogate, person-years were classified according to the most dangerous plant (in the order listed above) or the highest surrogate category the person had ever worked in 5 years prior to the time at risk. Because of indications that some workers were monitored for plutonium as a result of suspected diseases, person-years were classified as unmonitored until 2 years after the initial monitoring date. Of the 5860 radiochemical and plutonium plant workers (218 lung cancer deaths) indicated in Table 1 as monitored, 176 workers (29 lung cancer deaths) were monitored in the last 2 years of follow-up and thus considered as unmonitored in dose–response analyses. Most analyses were based on dose received 5 or more years before the time at risk. There were 14 categories for lagged cumulative internal lung dose, a zero dose category and 13 other categories with boundaries of 0.2, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5 and 6 Gy; unmonitored person-years were classified according to the plutonium surrogate. The same categories were used to classify cumulative external dose with an additional category for unmonitored workers. Because there was no evidence that workers who were not monitored for external exposure had risks that differed from workers with zero dose, these categories were combined into a single zero dose category for most analyses. Some analyses included evaluation of internal dose in exposure ''windows'' of 5–15 years, 15–25 years, and 25+ years prior to the time at risk; categories for these dose windows were the same as those for the 5-year lagged dose.

Analyses based on both excess relative risk (ERR) and excess absolute (EAR) models were conducted, although the ERR model analyses were more extensive. The age-specific risk, λ (*a, s, b, c, z, d*), where *a* is attained age, *s* is gender, *b* is birth cohort, *c* is calendar year period, *h* is age at hire, and *d* is dose, is defined as follows for the two models.

Excess relative risk model:

$$\lambda(a, s, b, c, h, d) = \lambda_0(a, s, b, c)[1 + ERR(a, s, h, d)]$$

Excess absolute risk model:

$$\lambda(a, s, b, c, h, d) = \lambda_0(a, s, b, c) + EAR(a, s, h, d)$$

The logarithm of the baseline hazard λ_0 (a, s, b, c) was modeled as a linear-quadratic function of attained age and gender, birth cohort (four categories), and calendar period (two categories). In addition, a parameter that allowed for differences in mortality for male main and auxiliary plant workers was included since there was evidence that male auxiliary plant workers had higher baseline rates. This model for the baseline risk was chosen after exploration of several alternative functions, including the use of gender-specific functions of attained age, finer categories for birth cohort and calendar year, and, for the ERR models, stratification on age, gender, and birth cohort or calendar period. These alternatives gave results for the *ERR* and *EAR* that are very similar to those reported previously.

ERR is the excess relative risk function and *EAR* is the excess absolute risk function, in which d involves both external and internal lung doses. The dose response model that is emphasized is as follows

$$\beta_{plu,S}d_{plu}I_{mon}\exp\left(\sum_k \alpha_{plu,k}z_k\right) + \beta_{ext,S}d_{ext}\exp\left(\sum_k \alpha_{ext,k}z_k\right) + \eta_j I_{unmon}\exp\left(\sum_k \gamma_{jk}w_{jk}\right), \quad (1)$$

where $\beta_{plu,S}$ and $\beta_{ext,S}$ are sex-specific parameters describing the respective external and internal dose–response slopes. The first two terms in Eq. (1) show linear functions of the time-dependent lagged internal lung (d_{plu}) and external doses (d_{ext}) given in grays. With ERR models, the parameters $\beta_{plu,S}$ and $\beta_{ext,S}$ indicate the ERR per gray, whereas with the EAR models, these parameters indicate the excess absolute risk expressed as excess deaths per 10,000 person-year Gy (PY-Gy). We also explored linear-quadratic functions, but in no case did the addition of quadratic terms for either internal or external dose significantly improve the fit of the model. For some analyses, conducted for descriptive purposes, categories of dose replaced the continuous variables. We also conducted analyses in which the term β_{plu} d_{plu} was replaced by the sum $\beta_{5–15}$ $d_{5–15}$ + $\beta_{15–25}$ $d_{15–25}$ + β_{25+} d_{25+}, where $d_{5–15}$, $d_{15–25}$, and d_{25+} indicate the internal dose to the lung in the respective exposure windows: 5–15, 15–25 and 25+ years from exposure. In these analyses, the sex ratio was assumed to be the same for all three windows.

The factors $\exp(\Sigma_k\ \alpha_{plu,k}\ z_k)$, $\exp(\Sigma_k\ \alpha_{ext,k}\ z_k)$, and $\exp(\Sigma_k\ \gamma_{jk}\ w_{jk})$ allow for modification of exposure effects by variables (z_k and w_{jk}) that included the logarithm of attained age, the square of this variable, and age at hire. Although tests of the need for each of these variables were conducted, final models were more selective as described in the Results section.

The η_j designate the excess relative or absolute risks for categories (indexed by j) of the plutonium surrogate index among the unmonitored, with categories 4 and 5 (Table 2) combined. The surrogate index was used for periods during which there was no plutonium monitoring data (I_{unmon} = 1) while internal doses to the lung (d_{plu}) were used during post-monitoring periods (I_{mon} = 1) for monitored workers. As noted above, persons are treated as unmonitored for the first 2 years after the initial monitoring date. Unmonitored workers in the auxiliary and reactor plants were treated as monitored with d_{plu} = 0 throughout their follow-up. Parameters associated with plutonium surrogate categories were constrained to be non-negative, except for the purpose of showing confidence intervals for these parameters. We also evaluated whether the coefficient β_{ext} depended on plutonium monitoring status; this was done by replacing the term β_{ext} d_{ext} with β_{ext1} d_{ext} I_{mon} + β_{ext2} d_{ext} I_{unmon} and testing whether β_{ext1} = β_{ext2}. For these analyses, it was assumed that the external dose coefficients were the same for the two sexes.

In all cases, parameter estimates were computed with maximum likelihood methods. Hypothesis tests and confidence intervals were based on likelihood ratio tests and direct evaluation of the profile likelihood. Two-sided P values are used throughout.

In addition to parameter estimates, we present estimates of the expected and excess cases, with the excess apportioned between internal and external exposures derived from the fitted models. These are calculated as described by Shilnikova *et al.* (*7*).

For the purpose of comparing findings from this study with those based on the Life Span Study (LSS) cohort of Japanese atomic bomb survivors, we analyzed LSS data for the follow-up period 1950–1997 using the data set that forms the basis of analyses in Preston *et al.* (*22*) and made available by the Radiation Effects Research Foundation (RERF). The LSS cohort includes a large proportion of atomic bomb survivors who were within 3 km of the hypocenters at the time of the bombings, and a similar-sized age- and sex-matched sample of people who were between 3 and 10 km from the hypocenters and is described in more detail by Preston *et al.* (*22*). For comparability with Mayak workers, our analyses were restricted to persons exposed between the ages of 15 and 60. Baseline risks for the LSS cohort were modeled as described by Preston *et al.* (*22*).

RESULTS

Table 3 shows the results of fitting models of the form shown in Eq. (1), in which the ERRs (column 2) or EARs (column 3) are linear functions of internal lung dose and external dose. Figure 1 depicts the dependence of the ERR and EAR on attained age. Because the ERRs and EARs are expressed on different scales for internal dose, external dose, and the plutonium surrogate, these are shown relative to their values at age 60. Both models indicate highly significant associations of lung cancer risks with both internal and external dose. No significant improvement in fit was brought about by adding quadratic terms for internal or external dose ($P > 0.4$ for both models and both doses). Both the ERR and EAR for internal dose depend on gender and attained age, although the nature of these dependences was different for the two models. Among those whose internal doses could not be estimated, risk increased with the ordered plutonium surrogate categories. The sections that follow discuss findings based on each of the models.

Results of Fitting Excess Relative Risk (ERR) Model

Lung cancer risk was found to be significantly associated with internal lung dose for both sexes ($P < 0.001$). The ERR per gray for females was estimated to be about 4.0 (95% CI: 1.9; 8.8) times that for males. There was strong evidence of a decline in the ERR with attained age (P = 0.004), which is depicted in Fig. 1. Risks at ages younger than 60 would be larger than those shown, while those at older ages would be smaller. For example, at age 50 the ERR per gray would be about 1.8 times the values shown, whereas at age 70 the ERR per gray would be about 0.6 times the values shown. We also evaluated categories of attained age. The male ERR per gray for internal dose for attained-age categories <55, 55–64, 65–74 and 75+ years with their 95% CI were respectively 7.5 (3.9; 13), 5.1 (3.3; 7.5), 2.5 (1.2; 4.3), and 0.9 (<0; 5.4). There was no evidence that the ERR per gray depended on age at hire (P > 0.5).

TABLE 3
Estimates of the Excess Relative Risk and the Excess Absolute Risk for Lung Cancer Mortality with 95% Confidence Intervals (CI) for Internal Dose to the Lung from Plutonium, External Dose, and Plutonium Surrogate Categories

Parameter and description	Excess relative risk (ERR) model	Excess absolute risk model
Internal lung dose[a]	ERR per gray at attained age 60	Excess deaths per 10^4 PY-Gy at attained age 60
Main effect per gray:		
Males	4.7 (3.3; 6.7)	115 (81; 156)
Females	19 (9.5; 39)	49 (29; 78)
External dose	ERR per gray (all attained ages)	Excess deaths per 10^4 PY-Gy at attained age 60
Main effect per gray:		
Males	0.17 (0.052; 0.32)	2.4 (0.56; 4.4)
Females	0.32 (<0; 1.3)	0.43 (<0; 1.6)
Plutonium surrogate categories[b,c]	ERR at attained age 60 (both sexes)	Excess deaths per 10^4 PY at attained age 60 (males[d])
Category 1	0.025 (<0; 0.17)	<0 (<0; 1.4)
Category 2	0.25 (0.08; 0.50)	2.8 (0.1; 7.5)
Category 3	0.54 (0.20; 1.0)	8.3 (2.6; 17)
Category 4: Males	1.7 (0.9; 2.8)	44 (21; 71)
Category 4: Females	11 (4.7; 25)	
Ratio of female and male coefficients:	1.0[e]	0.44 (0.2; 0.9)

[a] Based on persons who were monitored for plutonium or worked only in reactor or auxiliary plants.
[b] Based on persons who worked in radiochemical or plutonium plant and were not monitored for plutonium.
[c] See footnote to Table 2 for definitions of the plutonium surrogate categories.
[d] Estimates for females are 0.44 times these values.
[e] Except for category 4, there was no evidence that these ERR differed by gender.

There was no evidence that the ERR per gray for external doses depended on gender ($P > 0.5$), attained age ($P > 0.5$), or age at hire ($P = 0.38$). However, because of the known difference in baseline lung cancer rates for the two sexes, we nevertheless provide separate estimates for males and females; the ERR per gray for females was estimated to be 1.9 (95% CI: <0; 11) times that for males. Based on a model with no modification by gender or attained age, the P value for the association with external dose was < 0.001; for males alone, this P value was 0.002.

Although Table 3 and Fig. 1 show different dependences on gender and attained age for internal and external dose, in fact they did not differ significantly. In a model in which the modifying effects of gender and attained age were assumed to be the same for internal and external dose, the estimated ratio of the coefficients for internal (α-particle) and external (γ-ray) dose was 33 (95% CI: 14; 98). This can be regarded as an estimate of the relative biological effectiveness (RBE) of internal (α-particle) dose compared with external (γ-ray) dose.

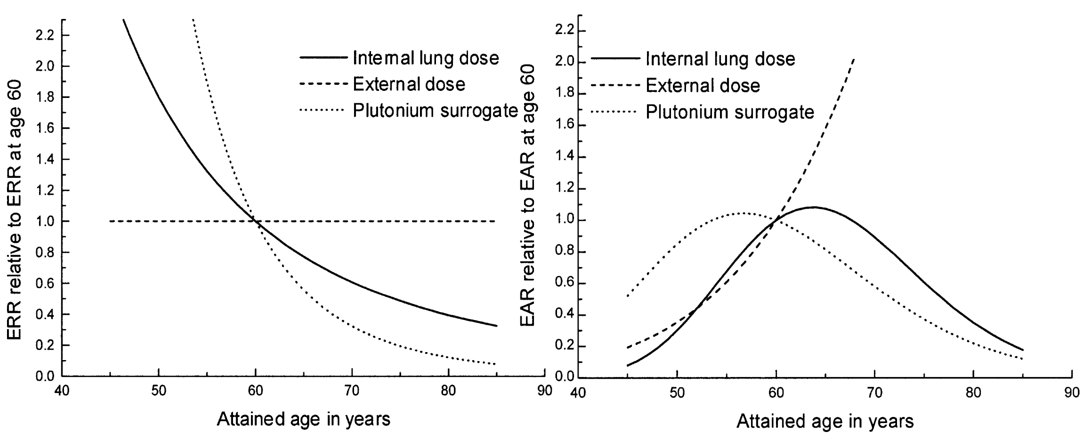

FIG. 1. Attained-age effects for internal lung dose, external dose, and plutonium surrogate. The panel on the left shows ERR per gray (ERR for surrogate) for lung cancer mortality as a function of attained age relative to its value at age 60. The respective functions for internal dose and the plutonium surrogate are $\exp[-3.2 \log (a/60)]$ and $\exp[-7.3 \log (a/60)]$, where a is attained age in years. For external dose, the function would be $\exp[-0.16 \log (a/60)]$, which is nearly indistinguishable from the function with no modification by attained age depicted in the figure. The panel on the right shows analogous functions of the EAR expressed as excess deaths per 10^4 PY-Gy (PY for surrogate). The respective functions for internal dose, external dose, and the plutonium surrogate are $\exp [2.6 \log (a/60) - 22 \log^2 (a/60)]$, $\exp [5.7 \log (a/60)]$, and $\exp [-1.5 \log (a/60) - 13 \log^2 (a/60)]$.

TABLE 4
Observed and Expected Deaths from Lung Cancer, and Estimated Excess Deaths Associated with Internal and External Exposure

	Person-years	Observed	Expected[a]	Excess: Internal exposure	Excess: External exposure
Males					
Internal α-particle dose					
Estimated as zero[b]	178,926	176	154.5 (91)	0 (0)	15.8 (9.3)
Estimated as positive[c]	52,546	167	73.5 (45)	72.1 (44)	18.2 (11)
Could not be estimated[d]	254,390	251[e]	161.8 (62)	72.9 (28)	25.3 (9.7)
Total	485,862	594	389.8 (66)	144.9 (24)	59.3 (10.0)
Females					
Internal α-particle dose					
Estimated as zero[b]	57,555	7	6.4 (91)	0 (0)	0.7 (9.3)
Estimated as positive[c]	17,476	24	3.8 (14)	20.9 (80)	1.6 (6.2)
Could not be estimated[d]	109,585	30[e]	11.4 (41)	13.8 (50)	2.5 (8.9)
Total	184,616	61	21.6 (35)	34.7 (57)	4.7 (7.8)

Note. Percentages are given in parentheses.
[a] Deaths that would have occurred in the absence of external or internal radiation exposure.
[b] Primarily persons who worked only in reactor or auxiliary plants.
[c] Primarily persons who worked in the radiochemical or plutonium plant and were monitored for plutonium.
[d] Worked in radiochemical or plutonium plant and not monitored for plutonium.
[e] Of these, 29 lung cancer deaths (27 males, 2 females) were monitored in the last 2 years of follow-up but were considered as unmonitored in statistical analyses.

Among workers who were not monitored for plutonium, statistically significant elevated risks were found in all but the lowest of the plutonium surrogate categories ($P = 0.005$ for category 2; $P < 0.001$ for categories 3 and 4), with the largest risks among females in the highest category. For the other categories, the ERR did not differ by sex ($P > 0.5$ in all cases). The ERR showed a decline with attained age that was even stronger than that estimated for monitored workers (Fig. 1). There was no evidence of modification by age at hire ($P = 0.35$).

Table 4 shows the predicted number of deaths associated with internal and external exposure and also shows the estimated number that would have occurred in the absence of exposure. In males, about 24% of the deaths are attributed to internal exposure and about 10% to external exposure. In females, about 57% of the deaths are attributed to internal exposure and about 8% to external exposure. For both males and females, the percentage of deaths attributed to internal exposure is higher among workers in the radiochemical and plutonium plants who were monitored for plutonium than for those who were not. This probably comes about at least in part because those with the highest doses were more likely to be monitored. In addition, the excess among the unmonitored workers is more likely to be underestimated because the surrogate index is not as reliable a measure of exposure as lung dose.

Results of Fitting the Excess Absolute Risk (EAR) Model

The third column of Table 3 shows estimated parameters for the EAR model. For internal lung dose, the ratio of EAR per 10^4 PY-Gy for females to that for males was 0.43 (95% CI: 0.24; 0.72). The comparable ratio for external dose was estimated, with considerable uncertainty, to be 0.18 (95% CI: <0; 1.1). For internal dose, both the logarithm of attained age and its square were needed to describe the dependence on attained age, and this resulted in the EAR increasing to about age 65 and then decreasing as depicted in Fig. 1. For external dose, the dependence could be described with the logarithm of attained age alone. Although Fig. 1 seems to indicate a markedly different pattern for internal and external dose at older ages, the pattern for external dose could not be estimated with certainty, and there was no evidence that the two patterns differed significantly. There was no evidence of dependence on age at hire for internal dose ($P > 0.5$). There was, however, modest evidence that the EAR for external dose might decrease with increasing age at hire ($P = 0.045$), although we did not include this dependence in our model.

Among workers whose internal doses could not be estimated, statistically significant elevated EARs were found in the three highest plutonium surrogate categories ($P = 0.042$ for category 2; $P < 0.001$ for categories 3 and 4). Modification by gender was similar to that among those whose internal doses could be estimated, with the ratio of EARs for females and males estimated to be 0.44 (95% CI: 0.20; 0.90). The EAR depended on attained age, and in this case increased until about age 55, and then decreased as depicted in Fig. 1. There was also evidence of a decrease in the EAR with age at hire ($P < 0.007$), and this was included in the Table 3 model.

TABLE 5
Numbers of Person-Years, Lung Cancer Deaths, and Relative Risks of Lung Cancer Mortality (with 95% CI) by Categories of Internal Dose to the Lung

	Males			Females		
Internal lung dose (Gy)	Person-years[b]	Lung cancers[b]	Relative risk (95% CI)	Person-years[b]	Lung cancers[b]	Relative risk (95% CI)
0[a]	178,542	176	1.00	57,555	7	1.00
>0–0.2	42,674	91	1.4 (1.0; 1.8)	13,671	3	0.91 (<0.91; 3.1)
0.2–1.0	7758	33	2.4 (1.5; 3.6)	2487	8	16 (6.1; 37)
1.0–3.0	1627	26	10.1 (6.3; 15)	804	2	15 (3.0; 38)
3.0–5.0	337	10	19 (9.5; 35)	172	1	
5.0+	151	7	33 (14; 67)	342	10	250 (110; 660)

[a] Referent group.
[b] Includes only person-years and deaths of those who were monitored for plutonium or worked only in reactor or auxiliary plants. The person-years and deaths not shown in this table were included in the analysis by estimating parameters for the ERR for each plutonium surrogate category as in Table 3.

Additional Results Based on the ERR Model

To further explore the dose response, we estimated the ERR for each of five categories of internal lung dose. These are shown in Table 5. For both males and females, risks increased with increasing lung dose, and risks were significantly elevated in all but the lowest positive dose category for females. In addition, we conducted analyses of data in restricted dose ranges. Evidence of a statistically significant response was found when analyses were restricted to internal doses less than 1 Gy ($P < 0.001$) and to internal doses less than 0.5 Gy ($P = 0.044$) but not when restricted to internal doses less than 0.2 Gy, although the risk coefficient was still positive. The failure to detect elevated risks may result simply from the reduced statistical power of these restricted analyses.

We also investigated the possible modifying effect of time since exposure for internal dose. In a model with no modification by attained age, the estimated ERR per gray (with 95% CI) for internal dose received 5–15, 15–25 and 25+ years before the time at risk were respectively −0.03 (<0; 12), 10.7 (3.8; 16), and 2.2 (0.2; 4.4), and this model fitted the data somewhat better ($P = 0.044$) than a model with a single coefficient. However, with attained age in the model, there was no evidence that the ERR per gray differed by time since exposure ($P = 0.38$), although the estimates for the three windows showed a similar pattern (−0.01, 8.2 and 4.4). Furthermore, the addition of attained age improved the fit of the model even when the ERR per gray was estimated separately for the three time-since-exposure periods indicated above ($P = 0.048$). The estimates for the three windows suggest that 15-year lagged dose might fit the data better than 5-year lagged dose; however, in fact, the deviances for the two models were similar. With a 15-year lag, the estimated ERR per gray for males at attained age 60 was 6.0 (95% CI: 4.1; 8.5).

To investigate whether the inclusion of workers in the radiochemical and plutonium production plants who were not monitored for plutonium might be distorting results, we conducted analyses that excluded these workers and person-years with results shown in the second column of Table 6. Because of the sparse data on external dose in this restricted data set, estimates of the ERR per gray for external dose were based on the two sexes combined. For internal dose, results are similar to those based on the full cohort (see

TABLE 6
Results of Lung Cancer Mortality Analyses Including Only Mayak Workers Who Were Monitored for Plutonium or Worked Only in the Reactor or Auxiliary Plants[a]

Parameter and description	All workers (374 lung cancer deaths)	Workers in the main plants who were hired before 1959 with information on smoking (278 lung cancer deaths)	
	Not adjusted for smoking		Adjusted for smoking
Relative risk for smoking[b]	—	—	9.6 (5.7; 17)
ERR per gray for internal dose			
Males	4.2 (2.8; 6.0)	4.3 (2.8; 6.3)	3.9 (2.6; 5.8)
Females	22 (9.5; 56)	17 (6.9; 45)	19 (7.7; 51)
ERR per gray for external dose			
Both sexes	0.10 (<0; 0.29)	0.065 (<0; 0.25)	0.027 (<0; 0.18)

[a] Workers in the radiochemical or plutonium plants who were not monitored for plutonium were excluded from these analyses.
[b] This is the relative risk of lung cancer for workers who smoked relative to workers who did not smoke.

TABLE 7
Estimated Parameters for Lung Cancer Mortality Risks with 95% Confidence Intervals (CI) for Internal Lung Dose in Mayak Workers and External Lung Dose in the Life Span Study (LSS) Cohort of Japanese Atomic Bomb Survivors Exposed between the Ages of 15 and 60

	Mayak workers			LSS cohort age 15–60 at exposure		
	Person-years[a] (percentage of total)	Lung cancer deaths[a]	ERR per sievert[b] at attained age 60[c] (95% CI)	Person-years (percentage of total)	Lung cancer deaths	ERR per sievert at attained age 60[c] (95% CI)
Total	306,505	374		1,797,201	1,130	
By sex						
Males	231,473 (76)	343	0.23 (0.16; 0.33)	566,926 (32)	622	0.40 (0.032; 0.86)
Females	75,032 (24)	31	0.93 (0.46; 1.9)	1,230,277 (68)	508	1.40 (0.76; 2.2)
Female/male ratio			4.0 (1.9; 8.8)			3.6 (1.2; 11)
By attained age			Excess deaths per 10^4 PY-Sv[b] (95% CI) (males[d])			Excess deaths per 10^4 PY-Sv (95% CI) (both sexes)
Under 55 years	209,332 (68)	63	1.4 (0.77; 2.3)	763,044 (42)	46	0 (<0; 0.53)
55–64 years	62,990 (21)	154	5.1 (3.5; 7.1)	442,429 (25)	167	1.5 (<0; 3.8)
65–74 years	29,558 (9.7)	133	5.2 (2.6; 8.6)	370,558 (21)	400	7.2 (3.4; 11.9)
75+ years	4,595 (1.5)	24	1.4 (<0; 12)	221,170 (12)	517	14.3 (6.6; 23.7)
Mean age	48	63		57	73	

[a] Including only person-years and lung cancer deaths where internal lung doses could be estimated; however, all workers and person-years were included in the analyses.
[b] Sieverts were calculated by dividing the dose in grays by a quality factor (QF) of 20.
[c] Based on a model in which the coefficient of the logarithm of attained age was set equal to −2.2.
[d] EAR for females would be a factor of 0.43 smaller than these estimates.

Table 3). However, for external dose, the ERR per gray was smaller than estimates based on the full data set and did not differ significantly from zero ($P = 0.12$).

To further investigate this, we conducted an analysis including all subjects but with separate estimates of the external dose ERR per gray for those with internal doses that could be estimated and for the remainder. The two estimates (for both sexes combined) were very similar: 0.16 (95% CI: 0.03; 0.35) and 0.18 (95% CI: 0.04; 0.37), respectively. The estimate of 0.16 per gray for those whose internal doses could be estimated is higher than that shown in the second column of Table 6. This difference appears to come about because, with the restricted data used in Table 6, baseline risks were estimated to be higher than in analyses based on the full data set.

We also conducted analyses that included data on smoking (ever/never classification), which are currently available for most main plant workers who were hired before 1959 and whose plutonium doses could be estimated. Among these workers, 74% of the males were identified as smokers, whereas only 3.4% of the females were identified as smokers. The third and fourth columns of Table 6 show results for this subgroup of workers with and without adjustment for smoking, which was carried out by including smoking status as part of the baseline risk. Adjustment for smoking reduced the ERR per gray for internal dose only slightly and did not greatly modify the female/male ratio of the ERR per gray. The estimated coefficient of the logarithm of attained age was also unchanged (–4.5 both with and without smoking adjustment). However, the smoking adjustment reduced the estimate of the ratio of the baseline risks for males and females from 11 to 2.0. Also, excluding auxiliary plant workers and workers hired after 1958 had little effect on the internal dose estimates as can be seen by comparing results in columns 1 and 3 of Table 6. Restriction of analyses to workers with smoking data reduced the ERR per gray for external dose and adjustment for smoking reduced it still further. However, confidence intervals were wide for these restricted analyses.

Results of Parallel Analyses of Data on Mayak Workers and Japanese Atomic Bomb Survivors

Table 7 shows the distribution of person-years and lung cancer deaths by gender and attained age for Mayak workers who had internal doses that could be estimated and for members of the Life Span Study (LSS) cohort of Japanese atomic bomb survivors who were 15–60 years old at exposure. For the LSS cohort, 68% of the person-years were in females, whereas the comparable percentage was 24 for Mayak workers. The LSS cohort is also older with 33% of the person-years over age 65, compared with 11% for the Mayak cohort. In comparing risks for the two cohorts, it is thus important to take account of dependences on gender and attained age.

When the ERR model was fitted to the LSS data, there was little evidence of modification by attained age. The estimated coefficient for the logarithm of attained age

(−0.36) was lower than that for internal dose in Mayak workers (−3.2), but the two coefficients did not differ significantly ($P = 0.12$). To compare ERR per sievert for the LSS and for internal dose in the Mayak cohort, we fitted models in which the coefficient of the logarithm of attained age was set equal to −2.2, obtained by weighting the cohort-specific estimates by their inverse variances, and a value that was compatible with the data from both cohorts. Results are shown in the top half of Table 7. For Mayak workers, estimates are expressed per sievert using a quality factor of 20 as recommended by the ICRP (*23*) for α-particle exposure. Estimates of the ERR per sievert based on A-bomb survivors are larger than those for Mayak workers, but there is considerable overlap in the confidence intervals. The ratios of the coefficients for females and males were similar for the two cohorts. The assumption of a larger RBE than 20, as estimated from the Mayak cohort, would make the Mayak estimates even lower.

When the EAR model was fitted to the LSS data, there was no evidence of dependence on gender ($P > 0.5$). The ratio of estimates for females and males was 1.3 (95% CI: 0.44; 4.0), higher than the ratio of 0.43 shown in Table 3 for internal dose in Mayak workers (P value for difference = 0.08). As with Mayak workers, the EAR depended on attained age, but the dependences in the two cohorts differed. For this reason, Table 7 shows EARs by categories of attained age. Results for the LSS cohort are for both sexes since there was no evidence that the EAR depended on gender. Results for Mayak are for males, and the EAR for females would be a factor of 0.43 smaller than the estimates shown in Table 7. For Mayak workers, there was clear evidence of risk from internal dose ($P < 0.001$) for all but the oldest age group. By contrast, for the LSS cohort, the strongest evidence of excess risk was for the two oldest age groups ($P < 0.001$), with little evidence of excess risk before age 55. For attained ages under 65, estimated risks for Mayak workers are significantly higher than those in the LSS cohort. Although risks for Mayak workers over age 75 are estimated to be smaller than those in the LSS, this might be because of the very limited data on Mayak workers in this age group.

For external dose in Mayak workers, modification by attained age was remarkably similar to that in the LSS cohort. There was little evidence that the ERR per sievert was modified by attained age in either cohort, and the EAR increased with attained age with nearly identical estimates of the coefficients of the logarithm of attained age (5.7 for Mayak; 5.8 for the LSS). Thus risk coefficients could be compared directly. For the LSS, the ERR per sievert for males (with no modification by attained age) was 0.29 (95% CI: 0.02; 0.62), while the EAR for both sexes at attained age 60 was 2.2 excess deaths per 10^4 PY-Sv (95% CI: 1.2; 3.6). These estimates are similar to those for external dose in male Mayak workers shown in Table 3 (ERR per gray = 0.17; EAR = 2.4 excess deaths per 10^4 PY-Gy).

DISCUSSION

As in previous analyses based on less extensive data, we found strong evidence that internal plutonium exposure increases lung cancer risks. Risk increased in a dose-dependent fashion among workers whose internal doses from plutonium exposure could be estimated, and, in addition, risk increased with the ordered plutonium surrogate variable among potentially exposed workers whose internal doses could not be estimated. The dose–response relationship was adequately described by a linear function, and there was evidence of risk when analyses were restricted to internal doses to the lung less than 0.5 Gy. The estimated ERR per gray for a male at attained age 60 was 4.7 (95% CI: 3.3; 6.7), very similar to the estimate of 4.5 obtained in the most recent analysis by Kreisheimer *et al.* (*14*), which was based on a subset of the data and did not include consideration of the modifying effect of attained age.

For internal plutonium exposure, the ERR per gray for females was estimated to be more than four times that for males. By contrast, the EAR per 10^4 PY-Gy for females was less than half that for males. The different patterns for ERR and EAR models reflect the very strong difference in baseline risks for the two sexes with baseline risks for males estimated to be about 11 times those for females; smoking differences explain much of this difference. Gender differences were also observed for the plutonium surrogate categories, where different mean doses for males and females in a given category might have contributed.

The ERR per gray and EAR per 10^4 PY-Gy for internal dose also depended on attained age. The ERR was found to decrease with attained age, especially among potentially exposed workers who were not monitored for plutonium. In this latter group, it was not possible to take account of the accumulation of dose with age and time since exposure. Analyses based on EAR models also revealed dependences on attained age. The EAR per 10^4 PY-Gy among those whose internal doses could be estimated increased with attained age to about age 65 and then decreased. With both ERR and EAR models, excess risks had declined to nonsignificant levels by the time workers reached age 75; however, data were very limited for evaluating risks at older ages (see Table 7). There was little evidence of modification by age at hire or time since exposure

We also found that external exposure increased lung cancer risks. This is in contrast to several earlier analyses of lung cancer risks (*10–14*) where there was little evidence of a dose response for external exposure. However, these earlier analyses did not include workers in the radiochemical and plutonium plants who were not monitored for plutonium, a restriction that excluded more than half the workers who had either external doses exceeding 1 Gy or external doses in the 0.1–1-Gy range (see Table 1). The use of the plutonium-potential variable allowed us to include these workers and thus provided a more powerful assessment of the effects of external dose, and we think this approach is more appropriate for the evaluation of external dose effects. Kreisheimer *et al.* (*14*) estimated the ERR per gray for external dose in males as 0.06 (95% CI: <0; 0.20), not incompatible with the estimate shown in Table 3, and similar to our results based on restricted data (Table 6). Our results for external dose are in agreement with analyses by Shilnikova *et al.* (*7*) of lung, liver and bone cancer risks (as a single category) with most of the deaths due to lung cancer. These analyses, which included the same workers as ours, also found a statistically significant association with external dose and no evidence of modification by gender, attained age, or time since exposure.

There is of course concern that the use of the plutonium-potential variable may not have provided an adequate adjustment for the effects of internal exposure. However, there is no direct evidence of this since the ERR per gray for external dose based on those whose plutonium doses could be estimated was similar to that based on those whose plutonium doses could not be estimated ($P > 0.5$). Nevertheless, analyses that were restricted to workers whose internal doses could be estimated (Table 6) yielded lower nonsignificant estimates of the effects of external dose, although their wide confidence intervals indicated they were compatible with estimates based on the entire cohort. Even in this group, uncertainties in plutonium dosimetry could lead to inadequate adjustment for internal exposure. External radiation exposure has been found to increase lung cancer risk in atomic bomb survivors (*22*), ankylosing spondylitis patients (*24*), Hodgkin's disease patients (*25*), and peptic ulcer patients (*26*). No association was found among tuberculosis patients who received protracted exposure from fluoroscopies, but these patients had underlying lung disease (*27*). Although we think that the identified association between external radiation dose and lung cancer mortality for Mayak workers is likely to be real, there is potential for bias in quantifying the dose–response relationship.

Parallel analyses of Mayak workers and the LSS cohort were also conducted. For external dose, even though one exposure was fractionated and the other acute, results were very similar both with respect to the estimated level of the ERR and EAR and the modifying effects of gender and attained age.

For internal dose, both the magnitude of the ERR per sievert and the sex ratio for the two cohorts were reasonably comparable. However, the ERR showed a strong decline with attained age in Mayak workers but not in the LSS cohort, although it is possible that this difference was due to chance. Pierce *et al.* (*28*) recently conducted analyses of lung cancer risks in a subset of the LSS that included data on smoking and found evidence for a strong decline in the ERR with attained age with the coefficient for the logarithm of attained age estimated to be -3.6, similar to the estimate of -3.2 for Mayak workers. They also found that the female/male ratio was reduced when smoking was taken into account.

Analyses of Mayak workers (internal dose) and the LSS based on the EAR model revealed differences in both the gender effect and the pattern of risk for attained age. For ages under 65, estimated risks for Mayak workers are significantly higher than those in the LSS cohort and may suggest that the relative biological effectiveness (RBE) is higher than 20.

Estimates of the RBE of dose from plutonium (relative to external dose) were also higher than the quality factor (QF) of 20 recommended by the International Commission on Radiological Protection (ICRP) (*23*), but the wide confidence intervals include the ICRP value. Estimates of the RBE are possibly less dependent on particular characteristics (including smoking patterns) of Russian workers than are the estimated ERR and EAR.

Patterns of baseline risks by gender, attained age, and birth cohort also differ in the LSS and Mayak cohorts, although we have not explored this in detail. However, we note that Preston *et al.* (*22*) estimate that baseline risks for LSS males are about 2.4 times those for LSS females, whereas baseline risks for Mayak males are about 11 times those for females. In the LSS cohort, the sex ratio for the ERRs is approximately equal to the sex ratio of the baseline risks, and thus the EARs for the two sexes are similar. In the Mayak cohort, the female/male ERR ratio is not as large as the male/female baseline risk ratio, and thus the EARs for Mayak females are smaller than those for males. Baseline rates for Mayak males are much higher than those for LSS males, a difference that reflects at least in part differences in smoking habits for the two cohorts. The average year of birth for Mayak workers was 1932, while that for LSS members exposed between the ages of 15 and 60 was 1910, a difference that likely contributes to different smoking patterns.

It may be more appropriate to compare Mayak risk estimates for internal plutonium exposure to estimates based on underground miners who, like Mayak workers, received protracted dose from α-particle emitters. In an analysis of lung cancer risks in eleven cohorts of male underground miners (*29*), the ERR per WLM (working level month) was found to decrease with increasing dose rate, attained age, and time since exposure. The ERR per WLM for exposure received 5–15 years ago at the lowest dose rate (<0.5 WL) at attained age 55–64 was estimated to be 0.034 per WLM. If it is assumed that 1 WLM is equal to 5 mGy (*30*, *31*), this would correspond to 6.8 per gray, slightly higher than the estimate of 4.7 per gray based on Mayak workers. Estimates for higher dose rates in the miners are smaller; for example, those exposed at 0.5 to 1.0 WL were estimated to have half the risk of those exposed at the lowest rate. For both Mayak workers and underground miners, the ERR decreased with increasing attained age. For the underground miners, the ERR per WLM for attained ages of 55–64, 65–74 and 75+ years relative to those for under age 55 were estimated to be 0.57, 0.29 and 0.09, respectively. Comparable ratios of ERRs for Mayak workers based on internal α-particle dose are similar, 0.67, 0.33 and 0.12, respectively. By contrast, we did not see the same pattern of decrease in the ERR with time since exposure that was observed for miners. Dosimetry limitations, especially the fact that it was not possible to measure the pattern of internal lung dose accumulation in individual workers, undoubtedly limited our ability to distinguish risks from dose received in different periods.

Several limitations of this study need to be noted and could potentially distort models developed in this paper. First, this a complex data set, and it is not simple to develop models that adequately describe the dependence of lung cancer risks on internal and external dose and also on gender, attained age, and age at hire. Our models are undoubtedly overly simple, but data do not support more detailed modeling.

An important limitation of most results presented in this paper is their failure to include data on smoking. Results for internal dose from analyses that were adjusted for smoking using the limited data that are now available did not differ greatly from analyses that were not so adjusted. Although adjustment for smoking lowered the estimated ERR per gray for external dose, this may have been due to chance given the wide confidence limits. The very high smoking rate in Russian men and the very low rate in Russian women make it unlikely that smoking is a strong confounder. Smoking undoubtedly contributes to the gender differences that were identified in our analyses, and it might also contribute to the pattern of risks with attained age. Efforts are currently under way to use medical records to improve data on smoking (including amount smoked) for the full cohort.

Another important limitation of our study relates to dose estimates. Estimating lung dose from exposure to plutonium and its pattern over time is challenging, and even dose estimates based on state-of-the-art dosimetry methods are subject to large uncertainties and potential biases. Smoking can influence the rate of clearance of plutonium from the lung, and current plutonium dosimetry models do not take account of this. Because of differences in smoking habits for males and females, dosimetry biases might thus affect estimates of risk coefficient ratios for the two sexes. External doses are less problematic, but dose estimates for early years are subject to biases resulting from limitations in the dosimeters used at that time. For example, film dosimeters used in the period 1948–1953 had no compensating filters for high-energy β particles, which could have led to overestimation of the external γ-radiation dose for some workers.

The ongoing collaborative Russian and U.S. dosimetry program continues to improve individual dose estimates for both external radiation and plutonium. In the near future, revised plutonium dosimetry will use physiologically based models of the fate of plutonium in the respiratory tract and in systemic tissues. These revised models will enable greater use of the unique autopsy data assembled at SUBI and will make it possible to address the potential influence of the worker's health status (smoking history, liver disease, etc.) on the distribution of plutonium in the body. Revised external dosimetry will take into account the limitations and sensitivities of the early dosimeters, make dose corrections for photon energy spectra and angular dependence at specific work locations, and provide new estimates of organ doses. Doses from the small amount of neutron exposure will also be estimated for specific work locations and occupations.

In spite of the limitations noted above, lung cancer risks from internal dose appear similar in many ways to such risks in underground miners who were also exposed to protracted α-particle radiation, whereas lung cancer risks from external dose are similar to such risks in A-bomb survivors. Clearly it is important to re-evaluate lung cancer risks making use of both improved dose estimates and smoking data.

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